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FISH & NEAVE IP GROUP
ROPES & GRAY LLP
ONE INTERNATIONAL PLACE
BOSTON, MA 02110-2624

EXAMINER	
RAWLINGS, STEPHEN L	
ART UNIT	**PAPER NUMBER**
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/649,591	MARKOWITZ, SANFORD D.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *75,84-91,93-106 and 123* is/are pending in the application.

4a) Of the above claim(s) *94 and 123* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *75,84-91,93 and 95-106* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 August 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20050228;20050525*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet*.

DETAILED ACTION

1. The election with traverse filed June 9, 2006, is acknowledged and has been entered.

Applicant has elected the invention of Group I, claims 75-107, drawn to a method for detecting colon neoplasia in a subject, said method comprising detecting the presence of one or more polypeptides in a sample acquired from the subject.

Applicant has further elected the species of the invention of Group I, wherein said one or more polypeptides is a polypeptide comprising an amino acid sequence that is at least 95% identical to SEQ ID NO: 3.

2. The amendment filed June 9, 2006, is acknowledged and has been entered. Claims 76-83, 92, and 107-122 have been canceled. Claims 75, 91, 94, 97-101, and 103 have been amended. Claim 123 has been added.

3. Claims 75, 84-91, 93-106, and 123 are pending in the application. Claims 94 and 123 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species of invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on June 9, 2006.

4. Claims 75, 84-91, 93, and 95-106 are currently under prosecution.

Information Disclosure Statement

5. The information disclosures filed February 24, 2005, May 23, 2005, October 12, 2005, October 14, 2005, October 28, 2005, and April 7, 2006, have been considered. An initialed copy of each is enclosed.

Election/Restrictions

6. Applicant's ground of traversal of the restriction and election requirement set forth in the Office action mailed May 3, 2006, is acknowledged. Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

Applicant has argued that search and consideration of claims drawn to the inventions of Groups I-VI would not constitute a serious burden because the amino acid sequence of SEQ ID NO: 21 is a portion of the amino acid sequence of SEQ ID NO: 3. Furthermore, Applicant has argued, with respect to the inventions of Groups I and II in particular, search and consideration of claims drawn to both inventions would not be a serious burden because a search of claims directed to one invention would largely overlap with the search necessary to examine claims directed to the other.

In response to Applicant's arguments, none of the pending claims are presently directed to the species of invention, wherein the one or more polypeptides is the polypeptide of SEQ ID NO: 21; therefore, at present, Applicant's first argument is moot. Nonetheless, the inventions of Groups I-VI are patentably distinct for the reasons set forth in the preceding Office action; because the inventions are distinct for these reasons, the search necessary to examine claims directed to any one of the inventions is not the same, nor is it coextensive with that necessary to examine claims directed to any other. Consequently, an examination of claims directed to any one of the inventions would necessitate a different search that that which would be performed to examine any other; and performing more than one search would be a serious burden. It is therefore proper to restrict the claims directed to the different inventions of Groups I-VI. With regard to the different species of the inventions of Group I, because each species is a process comprising measuring the presence (or amount) of one or more different polypeptides, the species are patentably distinct, each from the others, where the process comprises measuring the presence (or amount) of a different set of one or more polypeptides. As Applicant has elected the species of the invention, which is a process comprising measuring and/or quantifying the amount of a polypeptide comprising an amino acid sequence that is at least 95% identical to SEQ ID NO: 3, it is of no apparent consequence that the amino acid sequence of SEQ ID NO: 21 is a

portion of the amino acid sequence of SEQ ID NO: 3 because, as mentioned, none of the claims are presently directed to the polypeptide of SEQ ID NO: 21; and even so, contrary to Applicant's argument, the search necessary to examine claims directed to the elected species of invention would *not* suffice to permit examination of claims directed to a process comprising measuring or quantifying the polypeptide of SEQ ID NO: 21 because in the latter instance it would be particularly necessary to search the databases using SEQ ID NO: 21 as a query, rather than SEQ ID NO: 3.

For these reasons, the restriction and election requirement is deemed proper and therefore made FINAL.

Priority

7. Applicant's claim under 35 USC § 120 for benefit of the earlier filing date of the U.S. Patent Application No. 10/274,591, filed October 18, 2002, which claims benefit of U.S. Patent Application No. 10/299,345, filed August 26, 2002, is acknowledged.

However, claims 75, 84-91, 93, and 95-106 do not properly benefit under 35 U.S.C. § 120 by the earlier filing dates of the priority documents claimed, since those claims are rejected under 35 U.S.C. § 112, first paragraph, as lacking adequate written description and a sufficiently enabling disclosure.

To receive benefit of the earlier filing date under 35 USC § 120, the later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

In addition with particular regard to claims 86 and 87, even were the issues related to the insufficiency of the disclosure under 35 U.S.C. § 112, first paragraph, resolved, because the prior filed applications do not describe the practice of the claimed

invention using a biological sample derived from the inner wall and/or lumen of the intestinal tract, such as a stool sample removed from within the colon.

Accordingly, the effective filing date of claims 75, 84-91, 93, and 95-106 is deemed the filing date of the instant application, namely August 26, 2003.

Drawings

8. The drawing set forth as Figures 34, 35, and 41 are objected to because the figures depict nucleotide or amino acid sequences, which are not identified by sequence identification numbers, either in the figures or in the brief descriptions of figures at pages 16 and 18 of the specification. Sequences appearing in the specification and/or drawings must be identified by a sequence identifier in accordance with 37 C.F.R. 1.821(d); sequence identifiers for sequences appearing in the drawings may appear in the drawings or in the brief description of the drawings.

A replacement drawing sheet, including the correction, is required, if the drawings are objected to. See 37 CFR 1.121(d). However, this ground of objection would be withdrawn, so that a replacement drawing would be not be required, if Applicant were to amend the brief descriptions of the figures at pages 16 and 18 of the specification to include sequence identification numbers.

Specification

9. The disclosure is objected to for the following reason: The specification contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). Sequences appearing in the specification and/or drawings must be identified by sequence identifier in accordance with 37 C.F.R. 1.821(d). According to 37 CFR § 1.821(a), an unbranched sequence of four or more specifically identified amino acids or an unbranched sequence of ten or more nucleotides must be identified by sequence identification numbers. See MPEP § 2422.01.

In this instance, the sequences depicted in Figures 24, 25, and 41 are not identified by sequence identification numbers, either in the figures or in the brief descriptions of figures at pages 16 and 18 of the specification.

Applicant must provide appropriate amendments to the specification or drawings inserting the required sequence identifiers. Sequence identifiers for sequences appearing in the drawings may appear in the drawings or in the brief description of the drawings.

As noted in the attached Notice to Comply, appropriate action correcting this deficiency is required. If necessary to correct the deficiency, Applicant must submit paper and computer-readable copies of a substitute sequence listing, together with an amendment directing its entry into the specification and a statement that the content of both copies are the same and, where applicable, include no new matter.

10. The specification is objected to because the use of improperly demarcated trademarks has been noted in this application. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks. See MPEP § 608.01(v).

An example of such an improperly demarcated trademark is GenBank™, which appears in the specification at, e.g., page 33, line 29.

Appropriate correction is required. Each letter of a trademark should be capitalized or otherwise the trademark should be demarcated with the appropriate symbol indicating its proprietary nature (e.g., ™, ®), and accompanied by generic terminology. Applicants may identify trademarks using the "Trademark" search engine under "USPTO Search Collections" on the Internet at http://www.uspto.gov/web/menu/search.html.

Claim Objections

11. Claims 75, 84-91, and 95-106 are objected to because the claims are directed in the alternative to the subject matter of a non-elected invention. Nonetheless, because the claimed subject matter may be rejoined later during prosecution, Applicant need not remedy this issue at the present time.

With regard to claim 93, because the claim recites, "wherein the antibody interacts with an epitope of the amino acid sequence of SEQ ID No: 3", there is a presumption that the invention is a process for detecting colon neoplasia in a subject by detecting the presence of a polypeptide comprising an amino acid sequence that is at least 95% identical to SEQ ID NO: 3 in a sample acquired from the subject. Moreover, there is a presumption that claim 93 is not drawn to a process a process for detecting colon neoplasia in a subject by detecting the presence of a secreted polypeptide produced by expression of a nucleic acid having the sequence of SEQ ID NO: 5 in a sample acquired from the subject, so as to be drawn in the alternative to the subject matter of a non-elected species of invention.

Similarly, with regard to claim 94, which recites, "wherein the antibody interacts with an epitope of said polypeptide produced by the expression of the nucleic acid sequence set forth in SEQ ID NO: 5", is not a process for detecting colon neoplasia in a subject by detecting the presence of a polypeptide comprising an amino acid sequence that is at least 95% identical to SEQ ID NO: 3 in a sample acquired from the subject, so as to be directed to the subject matter of the elected species of invention.

12. Claim 75 is objected to because the claim recites, "for detecting whether a subject to likely to have a colon neoplasia". Appropriate correction is required, but it is suggested that this issue be remedied by amending the claim to recite, "for detecting whether a subject is likely to have a colon neoplasm".

13. Claim 85 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is

required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 85 depends from claim 84. Claim 84 is drawn to the invention of claim 75, wherein the biological sample is selected from the group consisting of (a) a blood sample and (b) a fraction derived from blood. Claim 85 recites, "wherein the biological sample is selected from among: whole blood, blood plasma, and blood serum". Plasma and serum are fractions derived from blood, but whole blood is not a fraction derived from blood; and while "whole blood" is a "sample of blood", it is not "a fraction derived from blood". A dependent claim must further limit each embodiment of the preceding claim; it not sufficient that a dependent claim only further limit one or another embodiment of the preceding claim. Appropriate correction is required.

14. Claim 90 is objected to because the claim recites, "a radioimmunoassays [sic]". Appropriate correction is required.

Claim Rejections - 35 USC § 112

15. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

16. Claims 75, 84-91, 93, and 95-106 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 75, 84-91, and 93, and 95-106 are indefinite for the following reason: Claim 75 is drawn to a process "for detecting whether a subject to [sic] likely to have a colon neoplasia [sic]". Presumably it was intended that the invention of claim 75 be a process for detecting whether a subject *is* likely to have a colon neoplasia by determining the presence of a secreted polypeptide comprising SEQ ID NO: 3 in a biological sample acquired from the subject, but according to the claim the presence of the polypeptide in the sample "is indicative of colon neoplasia", and not indicative of the

likelihood that a subject has a colon neoplasm. Is the invention a process for determining the likelihood that a subject has a colon neoplasm, or is it a process for detecting the presence of such a neoplasm in the subject? Because of the apparent lack of agreement between the purpose, as recited in the preamble, and correlative recited in the body of the claim, it is submitted that the metes and bounds of he subject matter that Applicant regards as the invention have not been delineated with the requisite degree of clarity and particularity to satisfy the requirement set forth under 35 U.S.C. § 112, second paragraph.

Claim 99 is indefinite because the claim recites the term "the subject's historical baseline". What is the subject's historical baseline? While the specification provides written support for the language of the claim, it does not describe with any particularity what value(s) represent the subject's historical baseline, nor how such value(s) are measured or determined; see paragraph [0025] of the published application[1]. Given the absolute lack of guidance and direction that might otherwise describe what value(s) represent "the subject's historical baseline", and how those value(s) are measured or determined, it is submitted that it is not possible to ascertain the metes and bounds of the subject matter that Applicant regards as the invention with the requisite degree of clarity and particularity to permit the skilled artisan to know or determine infringing subject matter, so as to satisfy the requirement set forth under 35 U.S.C. § 112, second paragraph.

Claim 100 is vague and perhaps indefinite for the following reason: Claim 100 depends from claim 75, which is drawn to a process "for detecting whether a subject to [sic] likely to have a colon neoplasia [sic]". If claim 75 is intended to be a process for detecting whether a subject *has* colon neoplasia by determining the presence of a secreted polypeptide comprising SEQ ID NO: 3 in a biological sample acquired from the subject, which according to the claim "is indicative of colon neoplasia", then it is unclear how the invention of claim 100 is practiced using the correlative recited therein, namely "wherein the presence of said at least one ColoUp2 polypeptide is indicative that the

[1] U.S. Patent Application Publication No. 2006/0035237 A1.

subject is likely to harbor a colon adenoma or a colon cancer". If the presence of the polypeptide is indicative of colon neoplasia in the subject, why would its presence indicate the likelihood that the subject harbors a colon adenoma or a colon cancer, as opposed to some other type of colon neoplasm? Does the process of claim 100, which provides an indication that the subject is likely to harbor a colon adenoma or a colon cancer, where the polypeptide is detected in the biological sample acquired from the subject, involve some other active step of which the process of claim 75 is not necessarily comprised that permits the determination of such an indication?

Claim 103 is vague and/or indefinite for the following reason: Claim 103 depends from claim 75, which is drawn to a process "for detecting whether a subject to [sic] likely to have a colon neoplasia [sic]". If claim 75 is intended to be a process for detecting whether a subject *has* colon neoplasia, or even for determining the likelihood that a subject has the disorder or disease, it is unclear why the invention of claim 103 would be practiced using a biological sample acquired from a subject *known* to have colon neoplasia (i.e., a subject currently receiving a therapy for colon cancer). In addition, if claim 75 is intended to be a process for detecting whether a subject *has* colon neoplasia by determining the presence of a secreted polypeptide comprising SEQ ID NO: 3 in a biological sample acquired from the subject, which according to the claim "is indicative of colon neoplasia", then it is unclear how the invention of claim 103 is practiced using the correlative recited therein, namely "wherein the presence of said at least one ColoUp2 polypeptide indicatives the subject is likely to have a relapse or a persistent or progressive colon cancer". If, in practicing the invention of claim 75, the presence of the polypeptide is indicative of colon neoplasia in the subject, why in practicing the invention of claim 103 would its presence then indicate the likelihood that the subject has a relapse or a persistent or progressive colon cancer? Does the process of claim 103, which provides an indication that the subject is likely to has a relapse or a persistent or progressive colon cancer, where the polypeptide is detected in the biological sample acquired from the subject, involve some other active step of which the process of claim 75 is not necessarily comprised that permits the determination of such an indication?

17. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

18. Claims 75, 84-91, 93, and 95-106 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a "written description" rejection.

The considerations that are made in determining whether a claimed invention is supported by an adequate written description are outlined by the published Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, para. 1, ``Written Description" Requirement (Federal Register; Vol. 66, No. 4, January 5, 2001). A copy of this publication can be viewed or acquired on the Internet at the following address: <http://www.gpoaccess.gov/>.

Claims 75, 84-91, 93, and 95-106 are directed to a genus of secreted polypeptides having an amino acid sequence of SEQ ID NO: 3.

An amino acid sequence of any particular amino acid sequence is understood to be any two or more contiguous amino acids of the particular amino acid sequence.

Accordingly, the claims are directed to a genus of secreted polypeptides, which vary substantially in structure and have no particular function, despite having an amino acid sequence comprising at least two contiguous amino acids of the amino acid sequence set forth as SEQ ID NO: 3.

Support for this interpretation of claims is found in the specification; see paragraph [0073] of the published application.

It appears the specification describes only one species of the genus of structurally and/or functionally variable polypeptides to which the claims are directed, namely the polypeptide of SEQ ID NO: 3, as it does not describe with any degree of

particularity, for example, any other polypeptides having amino acid sequences that are at least substantially identical (e.g., 95%) to the amino acid sequence of SEQ ID NO: 3. There is no disclosure that reasonably suggests that the single discloses species of the genus to which the claims are directed should be regarded as representative of the genus, as a whole, as, for example, the specification fails to describe any one particularly identifying (i.e., substantial) structural feature that is shared by the polypeptide of SEQ ID NO: 3 and other members of the genus, which correlates with any one particularly identifying functional feature, which is also shared by the polypeptide of SEQ ID NO: 3 and at least most other members of the genus.

Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, ``Written Description" Requirement (or hereafter "Guidelines") (cited *supra*) states, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). Guidelines further states, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species *cannot* be achieved by disclosing only one species within the genus" (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus. Because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described

distinguishing identifying characteristics sufficient to show that Applicant had possession of the claimed invention at the time the application was filed.

Furthermore, while the claims are not necessarily directed to polypeptides having amino acid sequences that are at least substantially identical to the amino acid sequence of SEQ ID NO: 3, even if they were, the description of those polypeptides would still not be sufficient to satisfy the written description requirement because the skilled artisan could not immediately envision, recognize or distinguish those polypeptides, the presence of which in a biological sample indicates the presence of colon neoplasia in the subject from whom the sample was acquired. Although the polypeptide of SEQ ID NO: 3 may be differentially expressed in colon cancer, the skilled artisan cannot predict which of the many other polypeptides to which the claims are directed are also over- or under-expressed in colon cancer.

Even among closely related protein family members, the skilled artisan cannot predict whether a particular member of the family is associated with the etiology or pathology a specific disease, solely on the basis that another member of the family has been shown to be. De Plaen et al. (*Immunogenetics.* 1994; **40**: 360-369) (of record; cited by Applicant), for example, reviews the structure, chromosomal localization and expression of twelve genes encoding members of the MAGE family of proteins; see entire document (e.g., the abstract). De Plaen et al. teaches six of the members of the gene family were found to be expressed at a high level in a number of tumors of various histological types; while five were very weakly expressed in all samples tested, and one, namely MAGE 7, was not transcribed at all in the ninety-five tumor samples tested (page 367, column 1). Just as not all members of the MAGE family of proteins are associated with cancer, particularly, since is it not obvious what, if any, association the weakly expressed MAGE proteins have, it is apparent that the skilled artisan cannot predict, based upon the information disclosed in the specification, whether variants of the polypeptide of SEQ ID NO: 3, as members of a presumed family of structurally related proteins, have an association with the etiology or pathology of colon cancer (e.g., whether the genes encoding such variants are overexpressed in colon cancer).

Considering the vastly different structures and functions of the members of the genus of polypeptides to which claims are directed, it is reasonably expected that the presence in a biological sample of most would not provide an indication of the presence of the disorder or disease, or of the likelihood that the subject has such a disorder or disease, since, for example, many of the polypeptides may not be expressed in the normal colon or even in colon cancer cells. Thus, any success in practicing of the claimed invention by determining the presence of any polypeptide other than the polypeptide of SEQ ID NO: 3 is largely unpredictable.

The Federal Circuit has decided that a patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated. See *Noelle v. Lederman*, 69 USPQ2d 1508 1514 (CA FC 2004) (citing *Enzo Biochem II*, 323 F.3d at 965; *Regents*, 119 F.3d at 1568).

"[G]eneralized language may not suffice if it does not convey the detailed identity of an invention." *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1892 (CAFC 2004). In this instance, as in that, there is no language that adequately describes with particularity the genus of secreted polypeptides comprising an amino acid sequence of SEQ ID NO: 3, the presence of any one of which in a biological sample indicates the presence of colon neoplasia in the subject from whom the sample was acquired. A description of how a material can be used, rather than of what it is, does not suffice to describe the claimed invention.

The Federal Circuit has indicated the relevant statute applies to all types of inventions. "Regardless whether a compound is claimed *per se* or a method is claimed that entails the use of the compound, the inventor cannot lay claim to the subject matter unless he can provide a description of the compound sufficient to distinguish infringing compounds from non-infringing compounds, or infringing methods from non-infringing methods". *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1894 (CAFC 2004). The claimed method depends upon finding secreted polypeptides comprising an amino acid sequence of SEQ ID NO: 3, the presence of which in a biological sample

indicates the presence of colon neoplasia in the subject from whom the sample was acquired; without such a polypeptides, it is impossible to practice the invention.

In addition, while perhaps the skilled artisan could potentially identify other secreted polypeptides comprising an amino acid sequence of SEQ ID NO: 3, the presence of which in a biological sample indicates the presence of colon neoplasia in the subject from whom the sample was acquired, it is duly noted that the written description provision of 35 U.S.C § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating (or practicing) it.

> The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed.*

Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (CAFC 1991). See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993); *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.,* 18 USPQ2d 1016 (CAFC 1991); *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1892 (CAFC 2004).

With further regard to claim 98, which is drawn to the method of claim 75, wherein the amount of the polypeptide in the sample is compared to "a predetermined standard", the value of the predetermined standard, which must be known to practice the claimed invention, has not been particularly described. The specification merely describes this value as "e.g., a known amount of purified ColoUp1 or ColoUp2 polypeptide"; see paragraph [0025] of the published application. Thus, the disclosure is not sufficiently descriptive of the value of the predetermined standard to which the claims are specifically directed to satisfy the written description requirement.

Finally with regard to claim 99, which is which is drawn to the method of claim 75, wherein the amount of the polypeptide in the sample is compared to "the subject's historical baseline", the disclosure is not sufficiently descriptive of the value that constitutes "the subject's historical baseline", and to which the claims are specifically directed, to satisfy the written description requirement. As explained in the above

rejection of claim 99 under 35 U.S.C. § 112, second paragraph, while the specification provides support for the language of the claim, it does not describe with any particularity what value(s) represent the subject's historical baseline, nor how such value(s) are measured or determined. Given the absolute lack of guidance and direction that would, if present in the specification, describe what value(s) represent "the subject's historical baseline", and how those value(s) are measured or determined, the written description requirement cannot have been met, as the specification would not reasonably convey to the skilled artisan that Applicant had possession of such subject matter at the time the application was filed.

19. Claims 75, 84-91, 93, and 95-106 are rejected under 35 U.S.C. 112, first paragraph, because the specification, **while being enabling for using** a process for detecting colon neoplasia in a subject, said method comprising detecting the presence of a secreted polypeptide comprising the amino acid sequence of SEQ ID NO: 3 in a sample acquired from the subject, wherein the presence of the polypeptide in the sample is indicative of the presence of colon neoplasia in the subject, **does not reasonably provide enablement for using** a process for a process for detecting whether a subject is likely to have colon neoplasia, said method comprising detecting the presence of a secreted polypeptide comprising an amino acid sequence of SEQ ID NO: 3 in a sample acquired from the subject, wherein the presence of the polypeptide in the sample is indicative of the presence of colon neoplasia in the subject. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

M.P.E.P. § 2164.01 states:

> The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Accordingly, even though the statute does not use the term "undue experimentation," it has been interpreted to require that the claimed invention be enabled so that any person

> skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors, which have been outlined in the Federal Circuit decision of *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), include, but are not limited to, the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed. See also *Ex parte Forman*, 230 USPQ 546 (BPAI 1986).

The amount of guidance, direction, and exemplification disclosed in the specification, as filed, would not be sufficient to enable the skilled artisan to use the claimed invention at the time the application was filed without undue and/or unreasonable experimentation.

As explained in the "written description" rejection above, the claims are directed to a genus of polypeptides that differ both structurally and functionally. As further explained above, the skilled artisan cannot predict, based upon the information disclosed in the specification, whether "variants" of the polypeptide of SEQ ID NO: 3 (i.e., polypeptides having an amino acid sequence comprising at least two contiguous amino acids of the amino acid sequence set forth as SEQ ID NO: 3), even as members of a presumed family of structurally related proteins, have an association with the etiology or pathology of colon cancer (e.g., whether the genes encoding such variants are overexpressed in colon cancer).

The specification teaches that the presence of the secreted polypeptide of SEQ ID NO: 3 in biological samples acquired from subjects is associated with the presence of colon adenoma or carcinoma in the subject; it, however, does not describe with any particularity any other polypeptide having an amino acid sequence comprising at least

two contiguous amino acids of the amino acid sequence set forth as SEQ ID NO: 3, which is similarly associated with such colon neoplasia.

Considering the vastly different structures and functions of the members of the genus of polypeptides to which claims are directed, it is reasonably expected that the presence in a biological sample of most would not provide an indication of the presence of the disorder or disease, or of the likelihood that the subject has such a disorder or disease, since, for example, many of the polypeptides may not be expressed in the normal colon or even in colon cancer cells. Thus, any success in practicing of the claimed invention by determining the presence of any polypeptide other than the polypeptide of SEQ ID NO: 3 is largely unpredictable. For this reason, the claimed invention could not be used without undue and/or unreasonable experimentation since it would first be necessary to identify other secreted polypeptides having an amino acid sequence comprising at least two contiguous amino acids of the amino acid sequence set forth as SEQ ID NO: 3, which are suitable markers for colon neoplasms, and then it would be necessary to elaborate the processes for detecting the presence of such neoplasms in a biological sample that involves the detection of those other polypeptides.

With further regard to claim 98, which is drawn to the method of claim 75, wherein the amount of the polypeptide in the sample is compared to "a predetermined standard", the value of the predetermined standard, which must be known to practice the claimed invention, has not been particularly described. Thus, the invention of claim 98 cannot be practiced.

Finally with regard to claim 99, which is which is drawn to the method of claim 75, wherein the amount of the polypeptide in the sample is compared to "the subject's historical baseline", the disclosure is not sufficiently descriptive of the value that constitutes "the subject's historical baseline", and to which the claims are specifically directed, to satisfy the written description requirement. As explained in the above rejections under 35 U.S.C. § 112, first and second paragraph, the specification does not describe with any particularity what value(s) represent the subject's historical baseline, nor how such value(s) are measured or determined. Given the absolute lack of

guidance and direction that would, if present in the specification, describe what value(s) represent "the subject's historical baseline", and how those value(s) are measured or determined, the he invention of claim 98 cannot be practiced.

In conclusion, upon careful consideration of the factors used to determine whether undue experimentation is required, in accordance with the Federal Circuit decision of *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the amount of guidance, direction, and exemplification disclosed in the specification, as filed, is not deemed sufficient to have enable the skilled artisan to use the claimed invention at the time the application was filed without undue and/or unreasonable experimentation.

Claim Rejections - 35 USC § 102

20. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

21. Claims 75, 84, 85, 89-91, 93, 95-97, and 100-106 are rejected under 35 U.S.C. 102(a) as being anticipated by WO 2002/268677 A1 (of record; cited by Applicant).

WO 2002/268677 A1 (Mack et al.) teaches a secreted polypeptide comprising an amino acid sequence of SEQ ID NO: 3; see entire document (e.g., page 249, SEQ ID NO: 23; and Table 25 at page 238; and Table 21 at page 221). Mack et al. teaches the gene encoding this polypeptide is up-regulated in colon cancer, as compared to its level

of expression in normal colon tissue; see, e.g., Table 21 at page 221. Mack et al. teaches detecting colon cancer in a subject by acquiring a biological sample (e.g., a sample of blood, serum, or stool) and determining if the secreted polypeptide is present in the sample using an immunoassay that employs a labeled or unlabeled antibody that binds to the polypeptide; see, e.g., pages 3, 5, 22, 23, 32, 33, 45-50, 52 and 53. Mack et al. teaches the process comprises quantifying the level of expression by measuring the amount of the polypeptide in the sample; see, e.g., page 51. Mack et al. teaches the immunoassay is an assay involving a Western blot, an immunoprecipitation assay, a radioimmunoassay, or an ELISA; see, e.g., page 53. Mack et al. teaches the antibody that is used in such assays, when labeled, is labeled using an enzyme, radioactive moiety, chromophore, or fluorescent or chemiluminescent substance; see, e.g., pages 15, 16, and 53. Mack et al. teaches the subject has either not been previously diagnosed or is currently receiving therapy for colon cancer; see, e.g.; page 3. Mack et al. teaches the process detects metastatic colon cancer, as well as precancerous or benign conditions, such as colon adenoma; see, e.g., pages 5 and 8. Mack et al. teaches the detection of the presence of the polypeptide in a biological sample aids in the determining the therapeutic protocol to be administered to a subject having colon cancer; see, e.g., pages 2-8.

22. Claims 75, 84, 85, 89-91, 93, 95-97, 100-103, 105, and 106 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Application Publication No. 2003/0077568 A1.

U.S. Patent Application Publication No. 2003/0077568 A1 (Gish et al.) teaches a secreted polypeptide comprising an amino acid sequence of SEQ ID NO: 3, which is overexpressed in colon cancer, as compared to its level of expression in normal colonic tissue; see entire document (e.g., SEQ ID NO: 2; the abstract). Gish et al. teaches the gene encoding this polypeptide is up-regulated in colon cancer, as compared to its level of expression in normal colon tissue; see, e.g., Table 1. Gish et al. teaches detecting colon cancer in a subject by acquiring a biological sample (e.g., a sample of blood) and determining if the secreted polypeptide is present in the sample using an immunoassay

that employs a labeled or unlabeled antibody that binds to the polypeptide; see, e.g., paragraph [0145]. Gish et al. teaches the process comprises quantifying the level of expression by measuring the amount of the polypeptide in the sample; see, e.g., paragraphs [0136], [0137], and [0152]. Gish et al. teaches the immunoassay is an assay involving a Western blot, an immunoprecipitation assay, or an ELISA; see, e.g., paragraphs [0137] and [0145]. Gish et al. teaches the antibody that is used in such assays, when labeled, is labeled using an enzyme, radioactive moiety, chromophore, or fluorescent or chemiluminescent substance; see, e.g., paragraphs [0093] and [0192]. Gish et al. teaches the subject has either not been previously diagnosed; see, e.g.; paragraphs [0014] and [0027]. Gish et al. teaches the process detects metastatic colon cancer; see, e.g., paragraph [0025]. Gish et al. teaches the detection of the presence of the polypeptide in a biological sample aids in the determining the therapeutic protocol to be administered to a subject having colon cancer; see, e.g., paragraphs [0016]-[0021].

Conclusion

23. No claim is allowed.

24. The art made of record and not relied upon is considered pertinent to Applicant's disclosure. Xin et al. (*Oncogene*. 2005 Jan 20; **24** (4): 724-731) teaches the secreted polypeptide of SEQ ID NO: 3, which is designated CCSP-2, is a novel candidate serological marker for colon neoplasia.

25. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on (571) 272-0832. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1643

slr
June 28, 2006

Continuation of Attachment(s) 6). Other: IDS:20051017(a);20051017(b); 2051031; 2060410; Notice to Comply

Notice to Comply	Application No.	Applicant(s)	
	10/649,591	MARKOWITZ, SANFORD D.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1643	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: If necessary to correct deficiency, Applicant must provide substitute copies of the Sequence Listing together with an amendment directing its entry and a statement indicating that both copies are the same and include no new matter.

Applicant Must Provide:

☐ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☐ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☐ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

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